

### **REMARKS**

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 13 and 15 to 16 and 18 to 23, the only claims pending and currently under examination in this application.

Claim 13 has been amended to incorporate the limitations of Claim 17, and Claim 17 has correspondingly been cancelled. Claims 15 and 16 have been amended to correct their dependency. Claim 16 has also been amended to correct a typographical error. Finally, Claim 22 has been amended to further specify the background probe sequences, support for this amendment being found in Table 1, page 37, Table 3, page 39, Table 5, page 42 and Table 10, page 53. As the above amendments introduce no new matter to the application and place the claims in better condition for allowance, their entry by the Examiner is respectfully requested.

The specification is objected to on the grounds that documents have been improperly incorporated by reference. The Examiner objects to the language at paragraph 36 of page 8 relating to relating to the incorporation by reference of all patents, patent applications and publications mentioned in the application. The Examiner asserts that the language "fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited references." The Applicants note that the documents cited in the instant application are incorporated by reference in their entirety and are not limited to specific portions or passages thereof.

In making this objection, the Examiner relies on *Advanced Display Systems*. As is demonstrated below, the Applicants respectfully submit that the cited case law cited in the Office Action is mischaracterized and does not, in fact, stand for the general principle alleged in the Office Action. Accordingly, the Applicants thus respectfully submit, as supported by the discussion below, that the instant situation is not analogous to that of *Advanced Display Systems, Inc.* Furthermore, the Applicants respectfully submit that the manner in which the documents of the instant application are incorporated by reference are

proper and thus the documents cited in the present application are properly incorporated by reference in their entireties.

The Office Action relies on *Advanced Display Systems, Inc.*, to support a general proposition that the specification must identify specific portions of a document incorporated by reference. The relevant issue in *Advanced Systems* concerned anticipation based not on a patent alone, but rather on the combination of the patent and the material potentially incorporated by reference therein. The issue thus was whether a magistrate judge committed legal error by instructing the jury to determine whether and what material was incorporated by reference into the patent. The court described generally the subject of incorporation by reference. In this description, the court noted “ To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents. See *In re Seversky*, 474 F.2d 671, 674, 177 U.S.P.Q. (BNA) 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement “clearly identifying the subject matter which is incorporated and where it is to be found”)”. It is this passage that the Office Action cites.

However, the situation of *In re Seversky*, the case cited in *Advanced Display*, is wholly different from the present situation. In the situation of *In re Seversky*, the Appellant attempted to incorporate by reference teachings of interest from a grandparent application. The parent application, was totally devoid of any reference to the teachings of interest, however the Appellant urged that the defect was cured because the grandparent disclosed the teachings and because the parent application is a continuation-in-part of the grandparent that disclosure was, ipso facto, incorporated by reference in the parent. In other words, the situation was one in which there was no “incorporation-by-reference” language whatsoever - a situation wholly different from the instant application which does include “incorporation-by-reference” language.

Accordingly, the Applicants submit that the documents cited in the instant application are properly incorporated by reference in their entireties. As such, the Applicants respectfully request the objection to the specification be withdrawn.

The Examiner has next objected to Claims 15 and 16 for improper dependency. In view of the above amendments to these claims, this objection may be withdrawn.

Next, Claims 13 and 15-23 have been rejected under 35 U.S.C. § 112, ¶ for an asserted lack of written description.

In making this rejection, in paragraph 8 of the office action, the Examiner asserts that the minimum number of exemplary background probes is not sufficient in view of the specification at paragraph 64 which states:

In a preferred embodiment, a background feature contains  $3.1 \times 10^6$  to  $6.3 \times 10^7$  background probes, preferably  $1.6 \times 10^7$  to  $4.7 \times 10^7$ , more preferably  $2.8 \times 10^7$  to  $3.5 \times 10^7$  background probes.

However, this section is speaking about the number of individual nucleic acid molecules that are present in a given background feature of a collection, not the total number of different background features that must be present in a given collection. As such, the specification need not disclose  $3.1 \times 10^6$  different background probe sequences in order to comply with written description, since this teaching of the specification is referring to the number of different (identical) molecules that are present in a given background feature, not the number of different background features that must be present in a given collection.

Furthermore, in paragraph 8 the Examiner questions the specification with respect to certain seq id nos, since they are longer than the recited length for background probes in the specification but nonetheless recited in certain of the claims as background features. In view of the above amendments to the claims, this particular issue is addressed.

In view of the above, it is submitted that the claims do comply with the written description requirement in that the claims are directed to methods of performing array assays with arrays that include background features and hybridization features, where the signals from background features are subtracted from the signals from hybridization features. The specification provides multiple representative examples, including working examples, of representative background features being employed in the claims methods, such that one of skill in the art would have no doubt that the applicant was in possession of the invention as claimed at the time the application was filed.

Next, Claims 13 and 15-23 have been rejected under 35 U.S.C. § 103 (a) as being unpatentable over Dehlinger in view of Fodor, Blanchard and Brink, and further in view of Iltia.

In making this rejection, the Examiner asserts that since Dehlinger suggests the use of negative control probes, Fodor and Blanchard disclose arrays of all possible oligomers of the lengths of probes of the present invention, Brink discloses the use of type I and type II control sequences that are designed to not hybridize to a target, and Iltia assertedly teaches sequences that do not specifically hybridize to their complement, the subject claims are obvious.

However, it is respectfully submitted that the combined teachings of the references fail to teach or suggest at least the following element of the claims.

All of the pending claims require that the background feature include probes that do not hybridize to any target in the sample being assayed.

None of the references teach or suggest, either alone or in combination, such a probe as a background probe. In fact, all of the mentioned negative control probe sequences in the cited references are ones that, based on known structure and sequence, are expected not to bind to their corresponding targets. For example, the type I probes in Brink are ones that are identical in sequence to their target but of opposite polarity. Prior to actual testing, such a sequence would be known not to hybridize to its corresponding target. Similarly, Brink's Type II probe is one that has the complementary sequence to its target but has the same polarity, i.e., the two sequences are complementary only if they are lined up or paired in the same direction, i.e., 5' to 3'. For example, where a target sequence in Brink is 5'-ATCG-3', the Brink Type II probe would have a sequence 5'-TAGC-3'. When these complementary strands of the same polarity are aligned, one obtains:

5'-ATCG-3'

3'-CGAT-5'

which clearly do not hybridize to each other. Again, prior to actual testing, such a sequence would be known not to hybridize to its target.

With respect to *litiä*, this reference fails to make up the above deficiencies for the following reasons. *litiä* has been cited by the Examiner as assertedly teaching probes that do not hybridize to their complementary sequence. However, the cited passage by *litiä* actually states:

"We repeatedly obtained lower hybridization signal with the probes designed against the sense strand of the target DNA (probe Eu14M). The reason for this is unknown."

This statement merely states that some probes gave **lower** signal than others, but not that they provide a signal which is representative of background signal such that the probes could be employed as background probes. Accordingly, *litiä* does not make up the fundamental deficiency in the primary four references as described above.

As such, for the above reasons, the cited references fail to teach or suggest the claimed methods.

Furthermore, with respect to Claims 22, this claim requires the presence of specific sequences as background features. Nothing in the cited references teaches or suggests that one must include these specific sequences. While Blanchard and Fodor may suggest a large number of sequences, there is no guidance in these references, or any of the other references, to select any of specifically recited sequences. Therefore the combined teachings of these references fails to teach or suggest these claims.

Claim 20 limits the background probes to ones that have specific characteristics, e.g., empirically observed inactive probes, reverse polarity nucleotide analogs, etc. The Examiner has not pointed to any location in the cited references where these specific characteristics are disclosed or suggested. Accordingly, the combined teaching of the references fails to teach or suggest these claims.

As such, none of the cited references teach or suggest the claimed invention and the rejection of Claims 13 and 15 to 23 as obvious under 35 U.S.C. § 103 (a) as being unpatentable over Dehlinger in view of Fodor, Blanchard and Brink, and further in view of *litia*, may be withdrawn.

Finally, Claims 13 and 25-23 have been provisionally rejected under the judicially created doctrine of obviousness type double patenting over Claims 50-52; 55-60, 62-64, 66-67, 71-73 and 76-84 of copending application serial no. 09/398,399. In view of the enclosed Terminal Disclaimer, this rejection may be withdrawn.

**CONCLUSION**

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078.

Respectfully submitted,

Date: 8.6.04

By:   
Bret Field  
Registration No. 37,620

enc:

- Terminal Disclaimer over application no. 09/398,399